THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 25

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte EDITH MATHIOWITZ
and ROBERT S. LANGER

Appeal No. 95-2876
Application 07/906,403[1]

ON BRIEF

Before WEIFFENBACH, PAK and ELLIS, Administrative Patent Judges.

PAK, Administrative Patent Judge.

DECISION ON APPEAL

[1] Application for patent filed July 1, 1992. According to appellants, this application is a continuation of Application 07/603,913 filed October 24, 1990, now abandoned, which is a continuation of Application 07/348,795 filed May 8, 1989, now abandoned, which is a continuation-in-part of Application 07/045,840 filed May 1, 1987, now U.S. Patent No. 4,861,627 granted August 29, 1989.

This is a decision on appeal from the examiner's refusal to allow claims 20 through 25, which are all of the claims remaining in the application.

Claims 20 and 25 are representative of the subject matter on appeal and read as follows:

20. Polymeric microspheres formed of a first and second polymer and a substance having a particle diameter of fifty microns or less incorporated in at least one of said polymers; wherein said first polymer forms a solid polymer core sphere not having drug as the core of the polymeric core that is coated with a single distinct layer of uniform thickness of the other polymer.

25. The composition of claim 20 wherein said substance is incorporated into one polymer, further comprising a second substance incorporated into the other polymer.

The references relied on by the examiner are:

Appelgren et al (Appelgren)	4,263,273	Apr. 21, 1981
Beck et al (Beck)	4,756,907	Jul. 12, 1988

The appealed claims stand rejected as follows:

(1) Claims 20 through 24 under 35 U.S.C. § 112, first paragraph, as the specification fails to set forth a best mode of carrying out the claimed invention;

(2) Claims 23 through 25 under 35 U.S.C. § 112, fourth paragraph, as failing to further limit the subject matter of their parent claims;

(3) Claims 20 and 22 through 24 under 35 U.S.C. § 103 as being unpatentable over the disclosure of Appelgren[2]; and

(4) Claim 25 under 35 U.S.C. § 103 as being unpatentable over the disclosure of Beck.

DISCUSSION

Rather than reiterate the conflicting viewpoints advanced by appellants and the examiner in support of their respective positions, reference is made to the Brief and the Answer for the full exposition thereof.

For the reasons set forth below, we will sustain only the last three rejections indicated above and, pursuant to the provisions of 37 CFR § 196(b), will enter a new ground of rejection against claims 20 through 23.

1. Preliminary Matter

[2] The examiner has withdrawn the rejection of claim 21 under 35 U.S.C. § 103 over the disclosure of Appelgren. See page 2 of the Answer.

As a preliminary matter, we note that appellants question the propriety of the examiner's refusal to enter an amendment after final rejection. We need to emphasize that appellants' remedy is through a petition to the Commissioner, not through an appeal to the Board. In re Hengehold, 440 F.2d 1395, 1403, 169 USPQ 473, 479 (CCPA 1971).

2. § 112, First Paragraph

The examiner has rejected claims 20 through 24 under 35 U.S.C. § 112, first paragraph. According to the examiner at page 4 of the Answer, the specification lacks the best mode of forming a particular microspherical product. The examiner, however, has not established that, at the time the application was filed, inventors **knew** of a mode of forming this microspherical product that they considered to be better than any other. Chemcast Corp. v. Arco Industries, 913 F.2d 923, 926, 16 USPQ2d 1033, 1035 (Fed. Cir. 1990). Since the examiner has not proffered any evidence of concealment

(accidental or intentional) of the best mode the inventors were aware of, the rejection cannot be sustained. We reverse.

3. § 112, Fourth Paragraph

We shall sustain the examiner's rejection of dependent claims 23 through 25 under 35 U.S.C. § 112, fourth paragraph. Appellants have not disputed that claims 23 through 25 fail to further limit the subject matter of their parent claims. See Brief in its entirety.

4. § 103 Based On Appelgren

The examiner has rejected claims 20 and 22 through 24 under 35 U.S.C. § 103 as being unpatentable over the disclosure of Appelgren.[3] The examiner states (see Answer, page 5) that:

> Comparing claim 20 to Appelgren et al., the patentees (esp. abstract; col. 2, lines 38-48; col. 3, lines 6-42; and Ex's. 1, 7 + 10-13) disclose spherical or nearly spherical solid pharmaceutical preparations for administration in dosage unit form

[3] Appellants submit at page 5 of their Brief that claims 20 and 22 through 24 do not stand or fall together. In response, the examiner argues that the claims do stand or fall together. See Answer, page 3. Since appellants do not contest the examiner's position, claims 20 and 22 through 24 will stand or fall together.

> comprising a pharmaceutically indifferent core, such as microcrystalline cellulose, and layer containing a pharmaceutical such as digoxin and a biodegradable polymer such as polyethylene glycol or hydroxy propylmethyl cellulose. While Appelgren et al. may not specify the particle diameter of the incorporated drug such as digoxin, choice of this parameter would be within the expected skill of a worker in the art, and thus obvious. The "particle diameter of fifty microns or less" for the incorporated substance has not been disclosed as, or shown to be, critical by applicants in the instant case.

Appellants do not dispute much of the examiner's findings of fact and conclusions as shown above. Appellants only argue that:

(1) Appelgren's examples do not suggest its pharmaceutically indifferent core to be a polymer (see Brief, page 14);

(2) Appelgren does not describe or suggest incorporating a substance (drug) in the core or the coating (see Brief, page 19); (3) Appelgren does not describe or suggest a uniform coating layer of polymer (see Brief, page 20); and

(4) Appelgren does not describe or suggest polymers having suitable phase separation properties (see Brief, pages 14 and 19). We are not persuaded by any of these arguments.

Appellants do not dispute that Appelgren teaches using microcrystalline cellulose, which is a carbohydrate polymer, as a pharmaceutically indifferent core. Rather, appellants argue that Appelgren's examples do not suggest its pharmaceutically indifferent core to be a polymer. In so arguing, appellants not only ignore that example 1 of Appelgren employs in its spherical granules microcrystalline cellulose, but they also fail to consider Appelgren as a whole, see In re Uhlig, 376 F.2d 320, 153 USPQ 460, (CCPA 1967). When Appelgren is considered as a whole, we agree with the examiner that it would have been obvious to one of ordinary skill in the art to employ a carbohydrate polymer, such as microcrystalline cellulose, as the pharmaceutically indifferent core of Appelgren's spherical granules.

Appellants argue that "Appelgren does not disclose or suggest incorporating a substance [i.e., a drug] in the **core** or the **coating**, as required by the instant claims." See Brief, page 19. Appellants, however, acknowledge that Appelgren's spherical granules contain "no drug...incorporated in the core or the coating, as required by the instant claims,

but rather in an intermediate layer." See Brief, page 14. We note that Appelgren's intermediate (first) layer containing a polymer and a drug, as indicated by the examiner at page 7 of the Answer, is included by the claimed coating polymer layer containing a substance (drug).

Appellants argue that Appelgren does not suggest forming a coating polymer layer of uniform thickness. In so arguing, appellants fail to consider Appelgren in its entirety. Appelgren, for example, indicates at column 3, lines 52-54, that the shape of the spherical or nearly spherical particles is dependent on the shape of the cores, not the intermediate (first) or second layers. This statement implies that the thicknesses of the intermediate and second layers are uniform or substantially uniform such that they do not affect the shape of the spherical or nearly spherical particles. The implication is further galvanized by Appelgren's requirement for "in vivo a sustained release". See column 3, line 63. To maintain a sustained release of a desired amount of a drug, it would appear that the thicknesses of the intermediate and second layers of Appelgren need to be uniform. In any event, since the types or thicknesses (amount) of polymers affect the

release of a drug encapsulated in the polymers (see column 3), it would have been obvious to one of ordinary skill in the art to provide a polymer layer having a uniform thickness to maintain the desired release rate for a given drug.

Appellants' arguments regarding phase-separation properties of the polymers and a phase-separation process for forming microspheres are also noted. However, none of the claims recites such limitations. When the claims do not recite the allegedly distinguishable features, "appellant[s] cannot rely on them to establish patentability." In re Self, 671 F.2d 1344, 1350, 213 USPQ 1, 7 (CCPA 1982).

5. § 103 Based On Beck

The examiner has rejected claim 25 under 35 U.S.C. § 103 as being unpatentable over the disclosure of Beck. The examiner states (see Answer, pages 5 and 6) that:

> Comparing claim 25 to Beck et al., the patentees (Fig's. 2 + 5; col. 3, lines 56-58 + 65-68; col. 8, lines 7-30; col. 9, lines 51-59; ¶ bridging col's. 9 + 10; col. 10, lines 26-38; and col. 12, lines 29-56) disclose microparticles or microspheres in which a core is formed of one pharmaceutical agent in a matrix surrounded by a

> shell of matrix material containing a second type of pharmaceutical. Beck et al. (¶ bridging col's. 9 + 10) suggest using <u>different</u> matrix materials. Beck et al. (col. 10, lines 36-38) contemplate microparticles ranging in size as low as 10 or 20 m [sic, Fm], so that size of the incorporated pharmaceutical would be even smaller. While the Beck et al. reference may not disclose a specific example of the above described embodiment, it is clearly within the purview of Beck et al., and thus would have been obvious therefrom to one skilled in the art at the time applicants' invention was made. Disclosure in a reference is not limited to its specific illustrative examples, but must be considered as a whole to ascertain what would be realistically suggested thereby to one of ordinary skill in the art. See <u>In re Uhlig</u>, 153 USPQ 460. Claim 25 permits incorporated substance(s) to be in both polymers, including the core polymers.

Appellants argue that Beck does not suggest forming a coating polymer layer of uniform thickness. In so arguing, appellants fail to consider Beck in its entirety. Beck, for example, evinces Figures 2 through 5 each showing spherical particles having a second polymer layer having a uniform thickness. Beck also describes a phase-separation process as one of the desired processes for making spherical particles which are shown in Figures 2 through 5. The phase-separation process described is inclusive of appellants' phase-separation

process for making appellants' spherical particles. Thus, it is our view that Beck describes spherical particles having a polymer layer of uniform thickness. In any event, since the types or thicknesses (amount) of polymers are known to affect the release of a drug encapsulated in the polymers, it would have been obvious to one of ordinary skill in the art to provide a polymer layer having a desired thickness (including uniform thicknesses) to maintain the desired release rate for a given drug.

Appellants' arguments regarding phase-separation properties of the polymers and a phase-separation process for forming microspheres are also noted. However, none of the claims recites such limitations. When the claims do not recite the allegedly distinguishable features, "appellant[s] cannot rely on them to establish patentability." In re Self, 671 F.2d 1344, 1350, 213 USPQ 1, 7 (CCPA 1982).

6. New Ground of Rejection

Under the provisions of 196(b), the following new ground of rejection is entered against claims 20 through 23.

Claim 20 through 23 are rejected under 35 U.S.C. § 102 as anticipated by, or in the alternative under 35 U.S.C. § 103 as being obvious over the disclosure of Beck.

Beck describes multi-layered microparticles which are useful for carrying pharmaceutical agents. See column 3, lines 55-68 in conjunction with Figures 2 through 5. Figure 5 specifically shows a spherical microparticle formed of a core of one particular pharmaceutical agent surrounded by a shell of matrix material containing a second type of pharmaceutical agent. See column 3, lines 65-68 in conjunction with column 10, lines 21-24. The core of the spherical microparticle of Figure 5 is prepared (column 9, lines 54-57) such that

> [t]he antigen or antibody alone can constitute the core of the microparticles or the antibody or antigen can dispersed in matrix material to form a core 11.

Beck then goes on to state (see the paragraph bridging columns 9 and 10):

> Moreover, while multi-layered microparticles such as the types shown in FIGS. 2, 4 and 5 are normally formed of a single type of matrix material, it is possible, if not desirable under some circumstances, to formulate contiguous layers of the microparticles from different matrix materials. Still further it is possible that under some circumstances, it may be desirable to deliver more than one antibody or antigen to the internal

> reproductive organs to treat more than one condition. Thus, for instance, monolithic microparticles could be prepared and delivered containing two different antibodies to passively treat two different diseases. In fact, it may be desirable under some circumstances to actively immunize a patient against one disorder and simultaneously passively immunize the patient against a second disorder with antigen and antibody delivered in the same microparticles.

The matrix materials employed to form the spherical microparticle are preferably selected from "polyglycolic acid, polylactic acid, as well as copolymers of glycolic and lactic acid, and glycerol mono-and distearate." See column 12, lines 42-45. The preferred size of the microparticle ranges from 20 to 60 micrometer (micron) which implies that a pharmaceutical agent incorporated therein is smaller than 60 or 20 microns. Since the phrase "wherein said first polymer form as a solid polymer core sphere **not having drug as the core of the polymeric core**" in claim 20 is

interpreted as including a pharmaceutical agent dispersed in a core matrix as long as it does not form the core of a core matrix, we are of the view that the subject matter of claims 20 through 23 is described by Beck as indicated supra. The extent to which such phrase is interpreted as excluding any pharmaceutical agent in the core matrix, we are of the view that it would have been obvious to one of ordinary skill in the art to eliminate one of the pharmaceutical agents, such as the one in the core matrix of Beck's multi-layered spherical microparticles, along with its attendant function. Compare In re Thompson, 545 F.2d 1290, 1294, 192 USPQ 275, 277 (CCPA 1976); In re Kuhle, 526 F.2d 553, 555, 188 USPQ 7, 9 (CCPA 1975). This is particularly true in the present situation since Beck also teaches that pharmaceutical agents can be incorporated "in a variety of configurations depending upon how the drug or drugs are to be released." See column 9, lines 60-64.

Any request for reconsideration or modification of this decision by the Board of Patent Appeals and Interferences based upon the same record must be filed within one month from the date hereof. 37 CFR § 1.197.

With respect to the new rejections under 37 CFR § 1.196(b), should appellants elect the alternate option under that rule to prosecute further before the Primary Examiner by way of amendment or showing of facts, or both, not previously of record, a shortened statutory period for making such response is hereby set to expire two months from the date of this decision. In the event appellants elects this alternate option, in order to preserve the right to seek review under 35 U.S.C. §§ 141 or 145 with respect to the affirmed rejection, the effective date of the affirmance is deferred until conclusion of the prosecution before the examiner unless, as a mere incident to the limited prosecution, the affirmed rejection is overcome.

If the appellants elect prosecution before the examiner and this does not result in allowance of the application, abandonment or a second appeal, this case should be returned to us for final action on the affirmed rejection, including any timely request for reconsideration thereof.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

37 CFR 1.196(b)

CAMERON WEIFFENBACH Administrative Patent Judge	)	
CHUNG K. PAK Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
JOAN ELLIS Administrative Patent Judge	)	

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